I claim:

1. A method of forming a high-resistance seal between a biological membrane and an electrode aperture in a partition separating an extracellular compartment from an intracellular compartment in a perfusion chamber, comprising the following steps:

delivering an extracellular solution with a biological membrane into said extracellular compartment;

withdrawing the extracellular solution from the extracellular compartment while preventing flow of extracellular solution into the intracellular compartment through the electrode aperture;

monitoring the position of the biological membrane in relation to the electrode aperture; and,

as the biological membrane approaches the electrode aperture, reversing the direction of fluid flow through the electrode aperture so as to attract the biological membrane to the electrode aperture and produce the formation of a seal between the biological membrane and the electrode aperture.

2. The method of Claim 1, further including the step of directing the extracellular solution and the biological membrane toward the electrode aperture.

3. The method of Claim 2, wherein said step of directing the extracellular solution and the biological membrane toward the electrode aperture is carried out by passing the extracellular solution and the biological membrane through a funnel structure having an opening facing the electrode aperture.

4. The method of Claim 3, wherein said step of withdrawing the extracellular solution from the extracellular compartment is carried out by withdrawing the extracellular solution through said opening facing the electrode aperture.

5. The method of Claim 4, wherein said step of withdrawing the extracellular solution through said opening facing the electrode aperture is performed by applying suction to the opening.

6. The method of Claim 1, wherein said step of preventing flow of extracellular solution into the intracellular compartment through the electrode aperture is performed by applying pressure to the intracellular compartment.

7. The method of Claim 6, wherein said step of reversing the direction of fluid flow through the electrode aperture so as to attract the biological membrane to the electrode aperture and to produce the formation of a seal between the biological membrane and the electrode aperture is carried out by changing said pressure to suction applied to the intracellular compartment.

8. The method of Claim 1, wherein said step of monitoring the position of the biological membrane in relation to the electrode aperture is carried out by sensing a change in electrical resistance across the electrode aperture.

9. The method of Claim 1, further including the step of monitoring a direction of fluid flow through the electrode aperture by sensing a change in electrical resistance across the electrode aperture.

10. The method of Claim 1, further including the step of providing suction from the intracellular compartment after the formation of said seal between the biological membrane and the electrode aperture to cause a rupture of the biological membrane.

11. The method of Claim 10, wherein said suction may be pulsatile.

12. The method of Claim 1, wherein said biological membrane includes an animal cell.

13. The method of Claim 2, wherein said step of directing the extracellular solution and the biological membrane toward the electrode aperture is carried out by passing the extracellular solution through a second aperture adjacent to the electrode aperture.

14. A patch-clamp electrode structure comprising:

a partition containing an electrode aperture between an extracellular compartment and an intracellular compartment;

a first fluidic channel adapted to deliver an extracellular solution with a biological membrane into said extracellular compartment;

a second fluidic channel adapted to withdraw the extracellular solution from the extracellular compartment; and

a third fluidic channel adapted to alternatively inject an intracellular solution into the extracellular compartment or withdraw the extracellular solution from the extracellular compartment through the electrode aperture.

15. The electrode structure of Claim 14, further including means for directing the extracellular solution and biological membrane toward the electrode aperture.

16. The electrode structure of Claim 15, wherein said means for directing the extracellular solution and biological membrane toward the electrode aperture comprises a funnel structure having an opening facing the electrode aperture.

17. The electrode structure of Claim 16, wherein said second fluidic channel is adapted to withdraw the extracellular solution through said opening facing the electrode aperture.

18. The electrode structure of Claim 17, wherein said second fluidic channel includes a source of suction for withdrawing the extracellular solution through said opening facing the electrode aperture.

19. The electrode structure of Claim 14, wherein said third fluidic channel includes a pressure source operatively coupled to the third fluidic channel.

20. The electrode structure of Claim 19, wherein said third fluidic channel further includes a suction source operatively coupled to the third fluidic channel.

21. The electrode structure of Claim 14, further comprising a means for detecting a change in electrical resistance across the electrode aperture.

22. The electrode structure of Claim 20, wherein said suction source is adapted to produce a rupture of the biological membrane.

23. The electrode structure of Claim 20, wherein said suction source is capable of operating in pulsatile fashion.

24. The electrode structure of Claim 15, wherein said means for directing the extracellular solution and biological membrane toward the electrode aperture comprises a second aperture adjacent to the electrode aperture and means for passing the extracellular through said second aperture.

25. A multi-chamber electrode assembly for electrophysiological recording comprising:

a chamber plate with a plurality of extracellular compartments;

a partition plate with a plurality of electrode apertures corresponding to and aligned with said extracellular compartments;

a foundation plate with a plurality of intracellular compartments corresponding to and aligned with said electrode apertures; and

fluidic channels for withdrawing fluid from the extracellular compartments.

26. The electrode assembly of Claim 25, wherein at least one of said extracellular compartments includes a funnel structure having an opening facing a corresponding electrode aperture, and said opening is connected to one of said fluidic channels.

27. The electrode assembly of Claim 26, wherein said foundation plate comprises fluid-flow conduits connected to said fluidic channels for withdrawing fluid from the extracellular compartments.

28. The electrode assembly of Claim 25, wherein said fluidic channels are formed by spacers creating a gap between the chamber plate and the partition plate.

29. The electrode structure of Claim 25, further including a second aperture adjacent to at least one of said electrode apertures, and wherein at least one of said fluidic channels is connected to the second aperture for withdrawing fluid from a corresponding extracellular compartment.

30. The electrode structure of Claim 25, wherein said chamber plate, partition plate, and foundation plate are an integral structure.

31. A method of fabricating a multi-chamber electrode assembly for electrophysiological recording comprising the following steps:

providing a chamber plate with a plurality of extracellular compartments;

providing a partition plate with a plurality of electrode apertures corresponding to and aligned with said extracellular

compartments;

placing spacers between said chamber plate and partition plate to form fluidic channels for withdrawing fluid therethrough from the extracellular compartments;

providing a foundation plate with a plurality of intracellular compartments corresponding to and aligned with said electrode apertures, said intracellular compartments including an electrode adapted for connection to electrophysiological recording equipment, and said foundation plate further comprising fluid-flow conduits aligned with said fluidic channels for withdrawing fluid from the extracellular compartments; and

stacking said foundation plate, partition plate, spacers and chamber plate so that corresponding intracellular compartments, electrode apertures and extracellular compartments are aligned to form independent perfusion chambers, and so that corresponding fluid-flow conduits and fluidic channels are aligned for each chamber.

32. The multi-chamber electrode assembly of Claim 31, wherein at least one of said extracellular compartments includes a funnel structure having an opening facing a corresponding electrode aperture in the partition plate, and said opening is adapted for fluid connection with said fluidic channels.

33. A method of fabricating a partition containing an electrode aperture for use between an extracellular compartment and an intracellular compartment in a perfusion chamber for electrophysiological recording, the method comprising the following steps:

etching a notch on a first side of a substrate of insulating material, wherein said notch does not perforate the substrate; and

etching a hole from a second, opposite side of the substrate to the notch, said hole having a diameter suitable for forming a high-resistance seal with a biological membrane.

34. A method of fabricating a partition containing an electrode aperture for use between an extracellular compartment and an intracellular compartment in a perfusion chamber for electrophysiological recording, the method comprising the following steps:

oxidizing a first side of a silicon substrate to form a layer of silicon dioxide;

depositing a layer of boron silicate glass over said layer of silicon dioxide;

removing all silicon material remaining unoxidized on a second, opposite side of the silicon substrate, thereby exposing a bottom side of said layer of silicon dioxide;

etching a hole on the bottom side of the layer of silicon dioxide, said hole extending through the layer of silicon dioxide

but not through the layer of boron silicate glass, the hole having a diameter suitable for forming a high-resistance seal with a biological membrane; and

etching a notch in the layer of boron silicate glass sufficiently deep to reach the hole and thereby produce a through perforation.